Respiratory Medicine (2012) 106, 184–188

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Intake of alcohol and risk of adult-onset asthma

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Received 10 October 2011; accepted 7 November 2011
Available online 29 November 2011

KEYWORDS
Asthma;
Alcohol;
Epidemiology;
Risk factor;
Population study;
Prospective

Summary
Aim: To examine the association between intake of alcohol and risk of adult-onset asthma.
Methods: Using data from two multidisciplinary questionnaire surveys we prospectively studied 19,349 twins, 12–41 years of age, from the nationwide Danish Twin Registry.
Results: The eight-year incidence of asthma was 4.3%. After adjustment for sex, age, BMI, physical activity, educational level and smoking, the risk of new-onset asthma was significantly related to overall alcohol intake in a U-shaped manner with the lowest risk observed in the group with a moderate weekly intake of alcohol (1–6 units/week), $p = 0.006$. The highest risk of asthma was observed in rare/never drinkers (<1 unit/month), OR = 1.59 (1.25–2.02), $p = 0.000$, whereas the risk of asthma in heavy daily drinkers (≥4 units/day) was also increased, however not statistically significant, OR = 1.13 (0.54–2.36), $p = 0.747$. The risk of new-onset asthma was lower for subjects with wine preference (3.3%) compared with beer preference (4.3%) or no preference (4.4%). After multivariable adjustment, wine preference was inversely related to incident asthma compared with beer preference. However, this finding was not statistically significant, OR = 0.87 (0.51–1.46), $p = 0.590$.
Conclusion: Alcohol intake is associated with new-onset asthma in adults with a U-shaped association between amount of alcohol intake and the risk of asthma.

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doi:10.1016/j.rmed.2011.11.004

Introduction

The prevalence of atopic diseases has increased substantially during recent decades. This increase is likely to have been caused by recent changes in lifestyle and environmental factors, but the causes are not yet fully understood. Alcohol has been a factor of interest, as several studies have suggested a link between alcohol consumption and atopy and risk of atopic diseases.[1–4] It is well-known that alcohol intake may trigger an asthmatic attack in subgroups of asthmatics[1,4] and experimental studies in rodents as well as in humans have shown that consumption of alcohol influences the immune system in several ways, e.g. by increasing the level of total serum immunoglobulin E (IgE),[5–8] and impairing the T-helper lymphocyte type 1 (Th1) immune response possibly favouring a relative Th2 dominance.[1,6,8,9] However, little knowledge exists on whether alcohol consumption causes development of new-onset asthma, and to our knowledge no prospective cohort studies have yet directly assessed the relationship between intake of alcohol and development of asthma. The aim of this study was to investigate the relationship between alcohol consumption and development of asthma later in life.

Methods

This prospective study used two multidisciplinary postal questionnaire surveys answered in 1994 and 2002, respectively, by a population-based sample of twins from the Danish Twin Registry, aged 12–41 years at baseline.[10] The response rates in the two surveys were 86 and 75%, respectively. At baseline (in 1994) 19349 subjects with no history of asthma were identified; 8701 (45.0%) males and 10,648 (55.0%) females, and these comprised the final study population. Subjects having new-onset asthma were defined as those answering "no" to the question "Do you have, or have you ever had asthma"? in 1994, but "yes" to the same question in 2002.

Alcohol consumption was assessed at baseline (in 1994) by dividing subjects into five categories based on self-reported responses to how many units of alcohol they consumed during a day, a week, or a month. The question used was "How much of the following do you drink?" The response categories were as follows: no or less than one unit per month (rarely drinkers), 1–3 units per month (monthly drinkers), 1–6 units per week (weekly drinkers), 1–3 units per day (daily drinkers), or ≥4 units per day (daily heavy drinkers). Preference of alcoholic beverage was assessed by dividing subjects into three categories corresponding to wine preference, beer preference and no preference, based on answers to how many units of wine and beer, respectively, they consumed. In order to qualify for either beer or wine preference the subject must have had an intake of wine or beer, respectively that exceeded the intake of the other beverage by at least two drinking frequency categories. Additional information on height, weight, smoking, quantity of leisure time physical activity and educational level of the study subjects were also collected at baseline through the questionnaire. Smokers were divided into ever and never smokers. Physical activity was divided into 1) light physical activity (subjects who spend less than 2 h per week on heavy exercise activities, 2) moderate physical activity (subjects who spend between two and 4 h on heavy exercise activities per week, and 3) high physical activity (subjects who spend more than 4 h per week on heavy exercise activities). Educational level was assessed by years of schooling.

Data were analysed with the statistical package SPSS 17.0 (SPSS Inc., Chicago, IL). Logistic regression was used to examine the association between asthma, alcohol intake and other risk factors. The logistic regression was performed

Table 1 Distribution of background factors in relation to alcohol intake among subjects, 12–41 years of age.

	Rarely drinkers <1 unit/month (n = 2860)	Monthly drinkers 1–3 units/month (n = 4631)	Weekly drinkers 1–6 units/week (n = 10,037)	Daily drinkers 1–3 units/day (n = 1205)	Daily heavy drinkers ≥4 units/day (n = 222)	Total (n = 18,955)
Age	20.6 (8.7)	27.1 (7.4)	28.7 (7.1)	32.3 (6.5)	34.0 (6.4)	27.4 (8.1)
Sex						
Male	995 (34.8)	1257 (27.1)	5111 (50.9)	946 (78.5)	207 (93.2)	8516 (44.9)
Female	1865 (65.2)	3374 (72.9)	4926 (49.1)	259 (21.5)	15 (6.8)	10,439 (55.1)
BMI	20.6 (4.2)	22.3 (3.8)	22.6 (3.1)	23.6 (3.4)	24.0 (3.5)	22.3 (3.6)
Smoking	463 (16.3)	1418 (30.7)	3728 (37.2)	650 (54.2)	157 (71.7)	6416 (34.0)
Physical activity						
Light	1146 (44.2)	2138 (50.4)	4477 (48.0)	548 (49.8)	85 (44.3)	8394 (48.1)
Moderate	745 (28.8)	1183 (27.9)	2777 (29.8)	304 (27.6)	45 (23.4)	5054 (29.0)
Heavy	699 (27.0)	922 (21.7)	2073 (22.2)	248 (22.5)	62 (32.3)	4004 (22.9)
Education	9.1 (2.4)	11.1 (1.9)	11.3 (1.8)	10.8 (2.0)	10.0 (1.9)	10.9 (2.1)
Alcohol preference						
Beer preference	0 (0)	139 (3.0)	2175 (21.7)	610 (50.6)	160 (72.1)	3084 (16.3)
Wine preference	0 (0)	0 (0)	492 (4.9)	41 (3.4)	5 (2.3)	538 (2.8)
No preference	2860 (100)	4492 (97.0)	7370 (73.4)	554 (46.0)	57 (25.7)	15,333 (80.9)

Sex, smoking, physical activity and alcohol preference are numbers (%); age (years), BMI (kg/m^2) and education (years) are means (SD). Figures are calculated from available data for the different variables.

Table 2 Incidence of asthma in relation to alcohol intake in subjects, 12–41 years of age.

Alcohol consumption	Asthma (%)	OR (95% CI)	*P*-value
Males			
12–18 years			0.193
<1 unit/month	37 (5.3)	2.42 (1.19–4.91)	0.015
1–3 units/month	11 (3.9)	1.75 (0.74–4.18)	0.206
1–6 units/week	10 (2.3)	1.00	
1–3 units/day	1 (4.3)	1.96 (0.24–16.03)	0.529
≥4 units/day	0 (0)	N/A	
19–41 years			0.418
<1 unit/month	16 (5.4)	1.70 (1.00–2.88)	0.050
1–3 units/month	34 (3.5)	1.07 (0.74–1.57)	0.713
1–6 units/week	152 (3.3)	1.00	
1–3 units/day	33 (3.6)	1.10 (0.75–1.62)	0.620
≥4 units/day	7 (3.5)	1.07 (0.49–2.31)	0.870
Females			
12–18 years			0.029
<1 unit/month	80 (8.7)	1.88 (1.15–3.09)	0.012
1–3 units/month	25 (4.9)	1.01 (0.56–1.83)	0.973
1–6 units/week	21 (4.8)	1.00	
1–3 units/day	0 (0)	N/A	
≥4 units/day	0 (0)	N/A	
19–41 years			0.001
<1 unit/month	51 (5.4)	1.42 (1.03–1.95)	0.034
1–3 units/month	152 (5.3)	1.39 (1.11–1.74)	0.004
1–6 units/week	174 (3.9)	1.00	
1–3 units/day	11 (4.4)	1.13 (0.61–2.11)	0.696
≥4 units/day	3 (23.1)	7.44 (2.03–27.28)	0.002

in three steps; first unadjusted, then adjusted for sex and age, and finally adjusted for all covariates, being sex, age, smoking, BMI, physical activity and educational level.

Results

At follow-up in 2002, a total of 838 (4.3%) new cases of asthma were identified, comprising 307 (3.5%) males and 531 (5.0%) females. Table 1 shows the distribution of background factors in relation to alcohol intake. Male sex, smoking, high BMI, physical activity and beer drinking was positively related to overall intake of alcohol.

The incidence of asthma in relation to intake of alcohol is shown in Table 2. There was a consistent U-shaped relationship between alcohol intake and the probability of acquiring asthma both in males and in females of adolescent (12-18 years) and adult age (19-41 years). The risk of new asthma was lowest among subjects with a moderate weekly intake of alcohol corresponding to 1-6 units/week and a consequently greater risk of asthma among subjects with a smaller and larger intake of alcohol, respectively. This effect was most pronounced among females, particularly in the oldest age group (19–41 years). Specifically, heavily drinking (≥4 units/day) women had an over sevenfold increased risk of asthma compared with women with a moderate weekly intake of alcohol (1-6 units/week). Due to the consistency of the nature of the relationship between alcohol intake and incident asthma in the different age groups and sexes we considered these categories together in subsequent analyses.

The results of the logistic regression analyses are shown in Table 3 with the incidence of asthma summed over age groups and sexes shown in Fig. 1. In the final analysis alcohol consumption was a statistically significant predictor for new-onset asthma, ($p = 0.006$). The highest risk of asthma was observed in rare/never drinkers (<1 unit/month), OR = 1.59 (1.25–2.02), $p = 0.000$, whereas the risk of asthma in heavy daily drinkers (≥4 units/day) was also increased, however not statistically significant, OR = 1.13 (0.54–2.36), $p = 0.747$. Furthermore, female sex and high BMI increased the likelihood of new asthma significantly, whereas age and educational level were negatively related to later onset of asthma. Smoking and physical activity were not significantly related to development of asthma.

The risk of new-onset asthma was lower for subjects with wine preference (3.3%) compared with beer preference (4.3%) or no preference (4.4%) (Table 3). After multivariable adjustment, wine preference was inversely related to incident asthma compared with beer preference. However, this finding was not statistically significant, OR = 0.87 (0.51 − 1.46), $p = 0.590$.

Discussion

The main finding of this study was an apparently U-shaped relationship between alcohol intake and risk of developing adult-onset asthma. The risk was especially high among subjects with no or rare alcohol consumption, compared with subjects who drink daily or weekly, indicating that

Table 3 Alcohol intake and risk of asthma in subjects, 12–41 years of age.

	Asthma (%)	Crude or (95% CI)	*P*-value	Adjusted OR[a] (95% CI)	Adjusted *P*-value	Adjusted OR[b] (95% CI)	Adjusted *P*-value
Alcohol consumption			0.000		0.000		0.006
<1 unit/month	184 (6.4)	1.86 (1.55–2.24)	0.000	1.67 (1.37–2.04)	0.000	1.59 (1.25–2.02)	0.000
1–3 units/month	222 (4.8)	1.37 (1.15–1.62)	0.000	1.26 (1.06–1.50)	0.010	1.24 (1.02–1.51)	0.031
1–6 units/week	357 (3.6)	1.00		1.00		1.00	
1–3 units/day	45 (3.7)	1.05 (0.77–1.44)	0.754	1.18 (0.86–1.63)	0.312	1.01 (0.71–1.43)	0.975
≥4 units/day	10 (4.5)	1.28 (0.67–2.43)	0.453	1.53 (0.80–2.92)	0.201	1.13 (0.54–2.36)	0.747
Alcohol preference			0.511		0.320		0.174
Beer preference	132 (4.3)	1.00		1.00		1.00	
Wine preference	18 (3.3)	0.77 (0.47–1.28)	0.317	0.68 (0.41–1.13)	0.140	0.87 (0.51–1.46)	0.590
No preference	688 (4.4)	1.02 (0.85–1.24)	0.814	0.92 (0.76–1.12)	0.416	0.80 (0.63–1.01)	0.062

[a] Adjusted for sex and age.
[b] Adjusted for sex, age, smoking, BMI, physical activity and years of education.

moderate alcohol consumption may protect against developing asthma. This effect was significant even when adjusting for possible confounders such as sex, age, smoking, BMI, physical activity and years of education. The risk of asthma among heavy drinkers was also increased compared with moderate drinkers but this proved to be statistically insignificant. However, there was an indication that particularly heavy-drinking women were at high risk of asthma, whereas this effect was not observed in men. One potential explanation for this could be that alcohol has a different impact on respiratory health in men and women but since only a small number of heavy-drinking subjects participated in the study there was insufficient statistical power to detect this effect. To support this explanation several studies have found that high and regular alcohol consumption is positively associated with aeroallergen sensitization.[7,11,12] The higher incidence of asthma among heavy drinkers seen in our study could therefore reflect a real increase in the risk of asthma in adults, particularly among women, who drink heavily.

To our knowledge no previous studies have shown a U-shaped relation between adult-onset asthma and alcohol intake, which limits our ability to compare results. However,

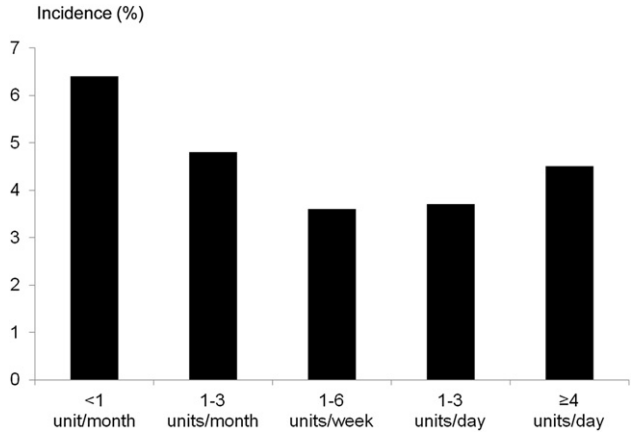

Figure 1 Eight-year cumulative incidence of asthma in relation to overall intake of alcohol among subjects, 12–41 years of age. For exact numbers and prevalence estimates, see Table 3.

several experimental and epidemiological studies have implied a relation between alcohol and asthmatic attacks, and studies on both rodents and humans have shown that alcohol influences the immune system, e.g. by increasing the total serum IgE and a possibly favouring a Th2-response.[1,3,6–8] Of particular interest is the findings by Linneberg et al. who found that the level of serum IgE depends on alcohol intake in a U-shaped manner, which resembles our findings closely.[7] They found that subjects drinking less than 3–4 units per week and subjects consuming above 10 drinks per week had higher levels of IgE compared with a middle group of subjects who consumed 5-10 drinks per week.

Of further interest is the earlier described J-shaped relation between alcohol consumption and risk of cardiovascular diseases[13] as well as the J-shaped relation between alcohol consumption and incidence of type 2 diabetes.[14] These findings are in accordance with our observations and indicate that some of the same underlying mechanisms could explain the effects of alcohol both on asthma, type 2 diabetes, and cardiovascular diseases. However, earlier suggested mechanisms of the effect of alcohol on type 2 diabetes and cardiovascular diseases are entirely different from one another and from the proposed mechanisms of action of alcohol on asthma. It could, nevertheless, be speculated that the commonalities lie in hitherto unexplored sociodemographic traits of the groups of people, who consume different quantities of alcohol - e.g. diet and other factors affecting health in general, rather than drinking-habits. Unfortunately, we did not have information on dietary intake, and therefore dietary intake could possibly have confounded our results. To elucidate this, further studies are needed.

Another finding of this study was that preference for wine drinking was inversely associated with risk of asthma, which could mean that wine drinking can actually protect against asthma. However, this finding was not statistically significant. Recently it has been suggested that alcoholic beverage-preference is associated with different lifestyles. A Danish study on shopping habits showed that wine drinkers tend to buy healthy goods similar to a Mediterranean diet, whereas beer-drinkers tend to be less health-conscious in their day-to-day shopping.[15] Several studies have pointed out that a Mediterranean diet may protect against development of health problems including asthma

due to a higher content of antioxidants.[16] As the healthier "wine drinkers' diet" could contribute to protection against asthma in itself, lifestyle could therefore confound our results in either direction. However, wine itself also contains antioxidants and studies suggest that an antioxidant-rich diet may have a protective effect on asthma.[17,18] Thus the natural antioxidant content in wine could contribute to this protective effect. On the other hand, previous studies have suggested that wine may trigger asthma attacks in certain individuals.[19] This effect has been attributed to the sulphites in wine although other factors such as hypersensitivity to traces of Hymenoptera venom antigens in wine may also be involved.[20,21] Taken together, we cannot conclude whether wine drinking is a protective factor per se or if it is simply the lifestyle of wine drinkers as a group that contributes to this finding.

We used self-reported asthma as the diagnostic approach. This allows some individual interpretation of questions and symptoms, as well as lack of recall regarding asthma in childhood, and may thus have given rise to an overestimation of the number of incident cases. Further it could be argued that questionnaires provide a chance of underreporting alcohol intake in general, but studies show that the subjectively reported alcohol intake corresponds to the ethanol-levels in blood.[6] Since we studied twins it can be argued that the results cannot be extrapolated to the population as a whole, although there is no data to support a differential effect of alcohol intake on the risk of asthma in twins and singletons. Furthermore, we measured educational level by years of schooling, which may be an unspecific indicator of socioeconomic status, particularly since the younger generations in general have longer educations and that years of schooling may not necessarily be associated with socioeconomic position. This may further imply that the adjustment for socioeconomic status in the multivariate analyses is incomplete and that there could be residual confounding by socioeconomic status. This could also explain, in part, the U-shaped relationship between alcohol intake and asthma and the protective effect of wine on asthma incidence although the observed effect of alcohol intake in this study was observed consistently both in adolescents and adults.

In conclusion, we found a significant association between alcohol intake and risk of adult-onset asthma. Notably, our results support a U-shaped relation between alcohol intake and risk of developing asthma, with moderate weekly drinkers having the smallest risk of asthma. This finding must be accommodated in the explanations of the recent increase in the prevalence of asthma but awaits further support from future prospective studies.

Conflicts of interest

None declared.

References

1. Linneberg A, Berg ND, Gonzalez-Quintela A, Vidal C, Elberling J. Prevalence of self-reported hypersensitivity symptoms following intake of alcoholic drinks. *Clin Exp Allergy* 2008;**38**:145—51.
2. Shimoda T, Kohno S, Takao A, Fujiwara C, Matsuse H, Sakai H, Watanabe T, Hara K, Asai S. Investigation of the mechanism of alcohol-induced bronchial asthma. *J Allergy Clin Immunol* 1996;**97**:74—84.
3. Thomsen SF, Ulrik CS, Kyvik KO, Larsen K, Skadhauge LR, Steffensen I, Backer V. The incidence of asthma in young adults. *Chest* 2005;**127**:1928—34.
4. Nihlen U, Greiff LJ, Nyberg P, Persson CG, Andersson M. Alcohol-induced upper airway symptoms: prevalence and co-morbidity. *Respir Med* 2005;**99**:762—9.
5. Gonzalez-Quintela A, Garrido M, Gude F, Campos J, Linneberg A, Lojo S, Vidal C. Sensitization to cross reactive carbohydrate determinants in relation to alcohol consumption. *Clin Exp Allergy* 2008;**38**:152—60.
6. Friedrich N, Husemoen LL, Petersmann A, Nauck M, Völzke H, Linneberg A. The association between alcohol consumption and biomarkers of alcohol exposure with total serum immunoglobulin E levels. *Alcohol Clin Exp Res* 2008;**32**:983—90.
7. Linneberg A, Petersen J, Nielsen NH, Madsen F, Frølund L, Dirksen A, Jørgensen T. The relationship of alcohol consumption to total immunoglobulin E and the development of immunoglobulin E sensitization: The Copenhagen Allergy Study. *Clin Exp Allergy* 2003;**33**:192—8.
8. Linneberg A, Roursgaard M, Hersoug LG, Larsen ST. Effects of alcohol consumption on the allergen-specific immune response in mice. *Alcohol Clin Exp Res* 2008;**32**:553—6.
9. Starkenburg S, Munroe ME, Waltenbaugh C. Early alteration in leukocyte populations and Th1/Th2 function in ethanol-consuming mice. *Alcohol Clin Exp Res* 2001;**25**:1221—30.
10. Skytthe A, Kyvik K, Bathum L, Holm N, Vaupel JW, Christensen K. The Danish Twin Registry in the new millennium. *Twin Res Hum Genet* 2006;**9**:763—71.
11. Linneberg A, Hertzum I, Husemoen LL, Johansen N, Jørgensen T. Association between alcohol consumption and aeroallergen sensitization in Danish adults. *Clin Exp Allergy* 2006;**36**:714—21.
12. Linneberg A, Nielsen NH, Madsen F, Frølund L, Dirksen A, Jørgensen T. Factors related to allergic sensitization to aeroallergens in a cross-sectional study in adults: The Copenhagen Allergy Study. *Clin Exp Allergy* 2001;**31**:1409—17.
13. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *BMJ* 2011;**342**:d671.
14. Koppes LL, Dekker JM, Hendriks HF, Bouter LM, Heine RJ. Moderate alcohol consumption lowers the risk of type 2 diabetes: a meta-analysis of prospective observational studies. *Diabetes Care* 2005;**28**:719—25.
15. Johansen D, Friis K, Skovenborg E, Grønbæk M. Food buying habits of people who buy wine or beer: cross sectional study. *BMJ* 2006;**332**:519—22.
16. Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. *J Allergy Clin Immunol* 2011;**127**:724—33.
17. Patel BD, Welch AA, Bingham SA, Luben RN, Day NE, Khaw KT, Lomas DA, Wareham NJ. Dietary antioxidants and asthma in adults. *Thorax* 2006;**61**:388—93.
18. Shaheen SO, Sterne JA, Thompson RL, Songhurst CE, Margetts BM, Burney PG. Dietary antioxidants and asthma in adults: population-based case-control study. *Am J Respir Crit Care Med* 2001;**164**:1823—8.
19. Vally H, de Klerk P, Thompson P. Important triggers for asthma. *J Allergy Clin Immunol* 2000;**105**:62—7.
20. Vally H, Thompson PJ. Role of sulfite additives in wine induced asthma: single dose and cumulative dose studies. *Thorax* 2001;**56**:763—9.
21. Armentia A. Adverse reactions to wine: think outside the bottle. *Curr Opin Allergy Clin Immunol* 2008;**8**:266—9.